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# The impact of chronic renal insufficiency on vascular surgery patient outcomes

*Derek P. Nathan*[a], *and Gale L. Tang*[a,b,*]

[a]*Division of Vascular Surgery, Department of Surgery, University of Washington, Seattle, WA*
[b]*VA Puget Sound Health Care System, Surgical Services 112, 1660 S. Columbian Way, Seattle, WA 98108*

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ABSTRACT

Renal insufficiency is associated with an increased incidence of poor outcomes, including cardiovascular events and death, in the general population. Renal dysfunction appears to have a particularly negative impact in patients undergoing vascular surgery and endovascular therapy. Although the exact mechanism is unknown, increased levels of inflammatory and biochemical modulators associated with adverse cardiovascular outcomes, as well as endothelial dysfunction, appear to play a role in the association between renal insufficiency and adverse outcomes. Outcomes after the surgical and endovascular treatment of abdominal aortic aneurysms, carotid disease, and peripheral arterial disease are all negatively affected by renal insufficiency. Patients with renal dysfunction may warrant intervention for the treatment of critical limb ischemia and symptomatic carotid stenosis, given the comparatively worse outcomes associated with medical management. Open repair of aortic aneurysms and carotid intervention for asymptomatic disease in patients with severe renal dysfunction should be performed with significant caution, as the risks of repair may outweigh the benefits in this population. Further study is needed to better delineate the risks of medical management for these conditions in patients with coexisting severe renal dysfunction. Lastly, current guidelines for the management of vascular diseases, including objective performance goals for critical limb ischemia, are likely not applicable in patients with severe renal insufficiency.



## 1. Introduction

Renal insufficiency has been shown to be an independent predictor of hospitalization, cardiovascular events, and death [1]. Understanding the effect of renal insufficiency in vascular surgery is critical, as renal dysfunction has been demonstrated to impact negatively on outcomes in patients undergoing vascular interventions [2–5]. This article reviews various aspects of the association between renal dysfunction and adverse vascular surgery outcomes. Glomerular filtration rate (GFR) is introduced as the best available method of measuring renal function. The importance of renal function as a preoperative and postoperative variable on surgical outcomes is then discussed. Potential explanations for the relationship between renal insufficiency and poor outcomes in vascular surgery are briefly presented. The literature on the effect of GFR on outcomes after vascular and endovascular surgery for aortic aneurysms, carotid stenosis, and peripheral vascular disease is then reviewed. Therefore, this article provides practitioners with an overview of the additional

*Corresponding author.
E-mail address: gtang@uw.edu (G.L. Tang).

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risks imparted by renal insufficiency on various vascular interventions. It remains difficult to determine whether those additional risks outweigh the benefits of intervention in the absence of better studies of the outcomes of medically managed patients with vascular conditions. The limited life expectancy of these patients should be taken into account for any procedures being considered for prophylactic reasons.

## 2. Renal dysfunction prevalence and definition

Renal insufficiency is prevalent in patients undergoing vascular surgery and endovascular interventions. The prevalence of renal insufficiency, defined as serum creatinine >2 mg/dL, in patients undergoing infrainguinal interventions for peripheral vascular disease has been reported to be >20% in a single-center study [6]. In a study of >8,000 patients in the National Surgical Quality Improvement Program who underwent repair of intact abdominal aortic aneurysms (AAAs), the prevalence of stage III chronic kidney disease (CKD) was 30%, while the prevalence of stage IV or V CKD was 7% [4]. A study from the Veterans Affairs National Surgical Quality Improvement Program of >20,000 patients who underwent carotid endarterectomy demonstrated that 31% of patients had stage III CKD, and 2% of patients had stage IV or V CKD [5]. Patients with impaired renal function currently represent a significant proportion of patients undergoing vascular surgery interventions. This proportion is likely to increase, given the increasing prevalence of type II diabetes and an aging population, emphasizing the importance of vascular surgeons and endovascular therapists being familiar with the increased risks of intervention in this population.

Historically, serum creatinine levels have been used to measure renal function. However, the association between serum creatinine and GFR is not linear, as GFR may decline to half the normal level before serum creatinine reaches the upper limit of normal [3,7]. As a result, serum creatinine is a poor reflection of actual renal function. GFR is considered to be the best available method of measuring renal function [8]. Initially, the Cockcroft-Gault equation was used to calculate an estimated GFR (eGFR) [9]. However, the equation derived from the Modification of Diet in Renal Disease (MDRD) study: $\text{eGFR} = 175 \times \text{Serum Cr}^{-1.154} * \text{age}^{-0.203} * 1.212$ (if patient is black) $* 0.742$ (if patient is female), has been shown to be more accurate, and has supplanted the Cockcroft-Gault equation. One limitation of the MDRD equation is that it underestimates GFR at higher levels of renal function [10]. A revised method of estimating GFR, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, was developed to addresses this issue [11]. Indeed, early studies support that the CKD-EPI equation may be better than the MDRD equation in estimating GFR in patients with normal renal function [10,12].

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines utilize GFR to classify CKD into five stages: stage I is GFR >90 mL/min/1.73 m$^2$ (patients with normal renal function but genetic or structural predisposition to renal disease or urine findings such as proteinuria or hematuria); stage II is GFR 60 to 90 mL/min/1.73 m$^2$; stage III is GFR 30 to 60 mL/min/1.73 m$^2$; stage IV is GFR 15 to 30 mL/min/1.73 m$^2$; and stage V is GFR <15 mL/min/1.73 m$^2$ [13]. This classification system is the most widely used and validated categorization of CKD. In the vascular and endovascular surgery literature, patients with stage I and II CKD have frequently been grouped together and categorized as having "mild or no" disease; patients with stage III CKD have been categorized as having "moderate" disease; and patients with stage IV and V CKD have been grouped together and categorized as having "severe" disease (Table 1). This simplified classification scheme and terminology will be used hereafter to describe renal dysfunction.

## 3. Impact of GFR on morbidity and morality

In a seminal study, the eGFR of 1 million adults was determined using the MDRD equation, and examined for its association with adverse outcomes [1]. After adjusting for risk factors, a history of cardiovascular disease, and proteinuria, a reduced eGFR was linked with an increased risk of hospitalization, cardiovascular events, and death. In addition, the study demonstrated that there was a graded association between decreasing levels of eGFR and these outcomes. As eGFR decreased to <60 mL/min/1.73 m$^2$, the rate of hospitalization, cardiovascular events, and death increased. This study corroborated the staging system utilizing GFR set forth by the National Kidney Foundation, and emphasized the importance of renal insufficiency, defined as GFR <60 mL/min/1.73 m$^2$, as a marker for increased morbidity and mortality [14].

## 4. Acute kidney injury after surgery and long-term survival

The majority of literature on renal dysfunction and surgical outcomes has focused on the effect of preoperative renal insufficiency on postoperative outcomes. Few studies have assessed the impact of acute kidney injury after surgery on long-term outcomes. In an important study addressing this issue, Bihorac et al [15] determined the relationship between acute kidney injury and long-term survival in >10,000 patients who were admitted to a surgical intensive care unit for at least 24 hours after major surgery. Acute kidney injury was defined by the RIFLE (risk, injury, failure, loss, and end-

**Table 1 – Stages of chronic kidney disease.**

| CKD stage | Description | GFR (mL/min/1.73 m$^2$) |
|---|---|---|
| I | Normal or mildly decreased GFR | ≥90 |
| II | Normal or mildly decreased GFR | 60–89 |
| III | Moderately decreased GFR | 30–59 |
| IV | Severely decreased GFR | 15–29 |
| V | Severely decreased GFR | <15 |

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.

stage kidney disease) classification, which uses percent change in serum creatinine or GFR [16]. This study found that acute kidney injury after surgery was associated with an independent long-term risk of death. In addition, there remained an increased risk of mortality in patients with acute kidney injury, even when there had been complete recovery of renal function by the time of hospital discharge. The authors concluded that patients with acute kidney injury merited close post-discharge follow-up due to their decreased long-term survival.

## 5. Potential explanations for association between renal insufficiency and poor outcomes

There are several possible explanations for the relationship between renal function and adverse events. First, renal insufficiency has been shown to accelerate cardiovascular calcification and atherosclerosis and alters vascular remodeling [17–20]. Patients with kidney dysfunction have higher levels of homocysteine and C-reactive protein, and lower levels of apolipoprotein A1, which have been associated with an increased risk for cardiovascular disease [21]. Increased inflammation can also play a role, as elevated levels of inflammatory biomarkers, including interleukin-6, tumor necrosis factor, and C-reactive protein, have been found in patients with renal insufficiency [22]. It is unclear whether this reflects impaired renal clearance of inflammatory biomarkers, or a causal role in acceleration of atherosclerosis and therefore worse outcomes [3].

Another important observation in the study of renal insufficiency and cardiovascular events comes from Chong et al [23]. In this study of patients with peripheral arterial disease, linear regression was used to determine the relationship between endothelial and renal dysfunction. Endothelial dysfunction was assessed by flow-mediated vasodilation, and renal dysfunction was measured by eGFR. This study found that renal dysfunction had a stronger relationship with endothelial dysfunction than hypertension, dyslipidemia, and coronary artery disease. The authors concluded that further investigation would be needed to evaluate whether the prevention of worsening of renal dysfunction might preempt further endothelial dysfunction, and thereby decrease the associated risk of cardiovascular events. Although the mechanism by which renal insufficiency portends worse outcomes has yet to be elucidated, there is ample literature from clinical studies, which will be discussed here, that demonstrates that GFR is an independent and powerful risk factor for poor outcomes in vascular patients.

Although the literature is not unanimous, there appears to be a benefit of statin therapy on renal-specific outcomes in patients undergoing endovascular surgery. A single-center study of 287 patients undergoing endovascular aneurysm repair suggested that statin therapy may prevent acute kidney injury [24,25]. It is possible that, through lowering peripheral vascular resistance, improving endothelial dysfunction, and reducing inflammation, statins exert renal protective effects and improve perioperative outcomes [26]. A single-center study of patients undergoing endovascular aneurysm repair failed to show any beneficial effect of statin therapy on postoperative estimated GFR or risk of GFR decline [27]. However, given the improvement in survival with perioperative statin use in patients undergoing vascular surgery, it is difficult to argue that vascular patients should not be on statin therapy [28,29].

## 6. Aortic aneurysms

The impact of renal insufficiency on the treatment of aortic aneurysms has been well described. Dr. Crawford's experience with the management of >1,500 thoracoabdominal aortic aneurysms is a seminal study in the management of this complex disease process [30]. This study is also noteworthy for its insightful examination of the role of preoperative kidney dysfunction on 30-day mortality, and the effect of postoperative renal complications on long-term survival. Despite the infrequent inclusion of patients with preoperative renal dysfunction (13% of the included patients), renal function still had a profound effect on postoperative outcomes. Higher preoperative renal creatinine predicted 30-day mortality by multivariate analysis, with patients with preoperative renal insufficiency experiencing a 30-day mortality of 13% compared with 7% ($P = .0072$) in those without preoperative dysfunction. This study also examined the impact of postoperative renal complications on long-term survival, and found that patients who sustained postoperative renal complications had a 5-year survival of 30% compared to 66% ($P <$ .0001) for those patients who did not. Of note, kidney failure, defined as postoperative creatinine level >3 mg/dL or need for dialysis, occurred in 18% of patients in this single-center of excellence experience. Although this study did not utilize GFR as a measurement of renal function, the results highlighted the importance of renal insufficiency on surgical outcomes after aneurysm repair for future investigations.

Azizzadeh et al [31] continued this work by investigating whether GFR was superior to serum creatinine in predicting outcomes after thoracic aortic aneurysm repair. The authors analyzed >1,100 thoracoabdominal aortic aneurysms and descending thoracic aortic aneurysms repaired between 1991 and 2004. GFR was estimated using the Cockcroft-Gault equation. Although both serum creatinine and eGFR predicted 30-day mortality, the latter was a much more powerful predictor of mortality. For example, patients with an eGFR >90 mL/min/1.73 $m^2$ had a 30-day mortality of 5%, compared to a 30-day mortality of >30% ($P = .0001$) in patients with an eGFR <30 mL/min/1.73 $m^2$. The authors concluded that GFR was superior to serum creatinine in identifying patients with subclinical renal disease who would not otherwise be classified as having renal insufficiency if serum creatinine were utilized to estimate renal function. The recommendation from these results was that elective repair of aneurysms involving the thoracic aorta should be undertaken with considerable caution in patients with severe renal insufficiency, and that these patients should be considered at high risk for surgical repair.

Data from the National Surgical Quality Improvement Program was used to evaluate the effect of CKD stage on 30-day mortality in >8,000 patients after endovascular (EVAR) and open repair of AAA [4]. Patients were assigned to CKD classes based on the National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines based on their eGFR calculated by the MDRD equation. Propensity score analysis was then used to match cohorts of patients with mild versus moderate and mild versus severe CKD. Patients with moderate versus mild CKD who underwent EVAR had higher rates of 30-day mortality (3% *v* 2%; $P = .013$) and complications (14% *v* 8%; $P < .0001$). Similarly, patients with moderate CKD who underwent open aneurysm repair had higher rates of 30-day mortality (8% *v* 3%; $P < .0001$) and complications (32% *v* 25%; $P = .001$). The differences in mortality and morbidity were even more dramatic when patients with severe CKD were compared with those with mild disease. Patients who underwent EVAR had increased 30-day mortality (6% *v* 3%; $P = .0081$) and complications (19% *v* 11%; $P < .0001$). Patients with severe CKD who underwent open repair of AAA had a 30-day mortality rate of 10% and a 40% rate of any complication. The suggestion from this study was that the diameter threshold for repair of AAA in patients with renal insufficiency be raised to >6.0 cm [4]. In addition, the authors concluded that the morbidity and mortality of open AAA repair in patients with severe CKD were significant enough that elective repair in such patients could not be recommended, except in "extenuating clinical circumstances."

Similar to the effect of postoperative renal complications on long-term outcomes after thoracoabdominal aortic aneurysm repair, the impact of postoperative acute kidney injury on 5-year survival after open AAA repair has also been demonstrated. A single-center's experience with open repair of infrarenal, pararenal, and extent IV thoracoabdominal aortic aneurysms was examined in order to determine predictors of decreased survival [32]. The impact of postoperative renal complication on long-term survival was one of the key findings of this study. Acute kidney injury after surgery was identified if the patient's postoperative renal function declined by at least one stage of CKD compared to their preoperative renal function. In this study of >400 open AAA repairs, the majority of which involved suprarenal and supraceliac clamps, 19% of patients had postoperative renal complications. Patients who had postoperative renal complications had a 5-year survival of 40% compared to 70% ($P = .004$) for patients who did not have postoperative renal complications. The development of techniques to decrease the incidence of postoperative renal complications in patients undergoing repair of complex aortic aneurysms was highlighted as an important area of future investigation.

The emergence, and growing dominance, of endovascular therapy in the management of aortic aneurysms has raised questions about the effect of this treatment modality on renal function. The Dutch Randomized Endovascular Aneurysm Management (DREAM) trial investigators performed a post-hoc analysis evaluating the impact of open and endovascular repair of infrarenal AAA on renal function [33]. After 5 years of follow-up, the mean eGFR was not significantly different between the open and endovascular repair groups (76 *v* 75 mL/min/1.73 $m^2$), and concluded that neither management option accelerated the loss of renal function. It is important to note that <10% of the patients included in the DREAM trial had renal disease. As preoperative renal insufficiency is one of the most powerful predictors of postoperative acute kidney injury, these findings are not necessarily applicable to many of the patients evaluated outside of this clinical trial [30].

While endovascular repair of infrarenal AAA appears to confer no increased risk of renal dysfunction, the repair of aortic aneurysms involving the renal arteries deserves closer and separate scrutiny. There are relatively few data on renal function after the endovascular repair of juxtarenal and pararenal aortic aneurysms. Haulon et al [34] reported on their experience with the endovascular repair of 80 juxtarenal, pararenal, and thoracoabdominal aortic aneurysms. In this multicenter experience, 11% of patients sustained postoperative acute kidney injury, defined as a decrease in eGFR of at least 30%. One patient required permanent dialysis. The recent publication of outcomes in patients with juxtarenal aortic aneurysms treated with a fenestrated endovascular graft offers additional insight [35]. In this multicenter study, 57 patients with juxtarenal AAAs underwent fenestrated EVAR. Although the study did not indicate how it defined preoperative renal insufficiency or postoperative renal complication, approximately 25% of the patients were reported to have preoperative renal insufficiency, with only 7% of patients being reported to have sustained perioperative acute kidney injury. Compared with rates of acute kidney injury that are approximately ≥20% after open repair of complex AAAs [32,36], these results suggest that the endovascular repair of complex aortic aneurysms may be particularly beneficial in decreasing postoperative renal complications and the associated decreased long-term survival [4,32]. Nonetheless, enthusiasm for the endovascular approach needs to be tempered until data on the long-term risk of renal occlusion and renal stent stenosis with this approach becomes available, and further studies show whether similar results can be achieved outside of centers of excellence with significant experience in fenestrated endografts [37].

## 7. Carotid disease

Outcomes after vascular and endovascular surgery for carotid stenosis are increasingly scrutinized. Identifying preoperative factors that predict worse outcomes after carotid interventions are particularly helpful and timely. Renal insufficiency has been identified as a risk factor for increased morbidity and mortality in patients undergoing carotid procedures. In a study utilizing the Veteran Affairs National Surgical Quality Improvement Program dataset, the effect of eGFR (calculated by the MDRD equation) on outcomes after carotid endarterectomy in 20,000 patients was evaluated [5]. Patients were divided into three groups based on eGFR, mild renal dysfunction, moderate renal dysfunction, and severe renal dysfunction. Outcomes included 30-day mortality and major complications, including neurologic, cardiac, pulmonary, and infectious. The study found that patients with moderate renal insufficiency were at increased risk of cardiac and pulmonary complications, and that patients with severe renal insufficiency were at increased risk of 30-day mortality, compared to patients with normal or mildly reduced renal function. The conclusion from the study was that renal insufficiency is an important and independent risk factor of poor outcomes after carotid endarterectomy. The 30-day mortality rate of 3.1% in patients with severe renal dysfunction was particularly noteworthy as the Asymptomatic Carotid Atherosclerosis Study demonstrated that patients with asymptomatic carotid artery stenosis will have a reduced 5-year risk of ipsilateral stroke if carotid endarterectomy is performed with <3% perioperative morbidity and mortality rate [38]. Future studies of the natural history, including the risk of stroke and death, of medically managed patients with renal insufficiency and asymptomatic moderate- and high-grade carotid stenosis are needed to determine whether the stroke risk reduction achieved by carotid intervention outweighs the increased risk in this patient group.

Given the improved outcomes with the medical management of asymptomatic carotid disease, it has been become increasingly important to identify patients who will and will not benefit from carotid revascularization. The Vascular Study Group of New England examined factors associated with 5-year survival after carotid endarterectomy in patients with asymptomatic internal carotid artery stenosis [39]. Dialysis dependence and GFR <60 mL/min/1.73 $m^2$ were two of several risk factors identified by multivariate analysis as predictive of decreased survival at 5 years. eGFR <60 mL/min/1.73 $m^2$ was a minor risk factor, while dialysis dependence was a major risk factor. Patients identified as high-risk had a 51% 5-year survival, compared to an 80% 5-year survival for patients identified as medium and low risk. Of note, only 5% of the patients included in the study were high risk. The authors concluded that the risk factors and prediction model derived from this analysis would be helpful in determining who would survive long-term after carotid endarterectomy and therefore benefit from the procedure.

Although carotid angioplasty and stenting has a different risk profile than carotid endarterectomy, including a lower risk of myocardial infarction and a higher risk of stroke, preoperative renal insufficiency remains a predictor of poor outcomes in patients undergoing carotid stenting [40]. Protack et al [41] evaluated the effect of renal dysfunction (as determined by eGFR calculated by the MDRD equation) on carotid angioplasty and stenting at a single-center during a 10-year period. Similar to previous studies, patients were divided into groups with normal renal function or mild renal dysfunction, moderate renal dysfunction, and severe renal dysfunction. Patients with severe renal dysfunction compared with patients with normal renal function and moderate renal dysfunction had worse 30-day mortality (15% *v* 1% and 3%; $P = .02$) and stroke (23% *v* 4% and 3%; $P = .01$) rates. Patients with moderate and severe renal insufficiency had 5-year survival rates <60%, compared to a 5-year survival rate of 87% ($P = .003$) for patients with normal renal function. These results suggest that severe renal dysfunction also has an adverse impact on perioperative outcomes after carotid angioplasty and stenting.

Although patients with renal insufficiency have worse outcomes after carotid interventions, it appears that patients with kidney dysfunction and symptomatic high-grade stenosis may fare even worse without intervention, and, therefore, may still benefit from revascularization [42]. In a re-analysis of the data from the North American Symptomatic Carotid Endarterectomy Trial, patients with symptomatic stenosis with stage III CKD (n = 524) were compared with patients with stage I and II CKD (n = 966). Patients with renal insufficiency who received nonoperative management had a higher ipsilateral stroke rate at 2 years (32%) compared to patients who received operative management (19%) ($P = .042$). Carotid endarterectomy significantly reduced the stroke risk with a number needed to treat of 4 for patients with stage III CKD, compared to a number needed to treat of 10 for patients with preserved renal function. The conclusion of this post-hoc analysis was that patients with stage III CKD and symptomatic high-grade carotid stenosis benefited from carotid endarterectomy [42]. Future studies are required to determine whether this provocative finding based on post-hoc analysis is borne out prospectively.

## 8. Peripheral arterial disease

Many patients with cardiovascular disease have both peripheral arterial disease and renal insufficiency, and several studies have examined the relationship between eGFR and outcomes after infrainguinal revascularization [3,43]. In a single-center study, 456 patients who underwent primary lower-extremity bypass surgery during a 10-year period at a single institution were stratified by eGFR, as calculated by the MDRD equation, into stages of CKD. Patients with severe renal insufficiency had a higher rate of the combined end-point of postoperative myocardial infarction and mortality. Long-term survival also differed by CKD stage. Due to similarities in hazard ratios, patients with stages I, II, and III CKD (eGFR >30 mL/min/1.73 $m^2$) were compared to patients with stages IV and V CKD (eGFR <30 mL/min/1.73 $m^2$). The 5-year survival for patients with an eGFR >30 mL/min/1.73 $m^2$ was 53% compared to 11% ($P < .0001$) for patients with an eGFR <30 mL/min/1.73 $m^2$. Employing the same groups for analysis, the authors found that the 5-year amputation-free survival for patients with an eGFR >30 mL/min/1.73 $m^2$ was 49% versus 8% ($P < .0001$) for patients with an eGFR <30 mL/min/1.73 $m^2$. These findings suggest that an eGFR <30 mL/min/1.73 $m^2$ is a powerful predictor of perioperative myocardial infarction and death, as well as long-term mortality and amputation in patients undergoing infrainguinal bypass surgery for peripheral vascular disease [3].

Renal insufficiency appears to impart a similar adverse effect in percutaneous interventions for infrainguinal peripheral arterial disease. The impact of CKD on perioperative and late outcomes was examined in a retrospective study of 879 patients who underwent endovascular therapy for lower-extremity peripheral arterial disease at a single institution during an 8-year period; 14% of these patients had severe CKD [43]. Similar to the findings from open revascularization, an eGFR <30 mL/min/1.73 $m^2$ predicted worse outcomes. Five-year survival in patients undergoing percutaneous peripheral vascular interventions was 24% in patients with eGFR <30 mL/min/1.73 $m^2$ versus 69% in patients without severe CKD ($P < .05$). Freedom from amputation at 2-years was 80% in the eGFR <30 mL/min/1.73 $m^2$ group compared to 97% in the other group ($P < .001$). There were no amputations observed after 2 years. Of note, approximately 30% of the patients in this study had claudication and, therefore, less advanced peripheral arterial disease. Although patients with stage V CKD are not included in the objective performance goals of critical limb ischemia, the finding that patients with an estimated GFR $<30$ mL/min/1.73 $m^2$ had a 1-year survival of 69% is significant, especially in the context of the objective performance goal of 80% 1-year survival [44]. Objective performance goals for critical limb ischemia require modification to reflect the poorer outcomes of patients with stage IV and stage V CKD.

These studies highlight the adverse effect of severe CKD on outcomes after surgical and endovascular interventions in patients with peripheral arterial disease. However, other treatment strategies may be associated with even worse outcomes than surgery or endovascular therapy in patients with severe CKD and peripheral vascular disease. Ortmann et al [45] examined the potential survival benefit of revascularization versus medical therapy in patients with critical limb ischemia and various stages of renal function. In this study of almost 400 consecutive patients with critical limb ischemia, patients were classified as receiving either revascularization or medical therapy based on the primary therapeutic decision made at the patient's initial presentation. Approximately one-quarter of patients were treated with medical therapy. Of the roughly three-quarters of patients who underwent revascularization, approximately 70% were treated with endovascular therapy, and 30% were managed with bypass surgery. This study is limited by patient-selection bias, as toe pressure and transcutaneous oxygen pressure were lower in the medical therapy cohort, suggesting more advanced atherosclerotic disease. Other risk factors were similar between the two groups. After adjusting for risk factors, primary revascularization resulted in improved survival compared to primary medical therapy in all patients included in the study. In particular, patients with severe renal insufficiency experienced a survival benefit with primary revascularization versus medical therapy. Of note, limb salvage was not improved by revascularization in patients with severe CKD. One-year mortality in all patients in this cohort study was 30%, with a 1-year mortality of 49% in patients with severe renal dysfunction, highlighting the challenges encountered when treating patients with peripheral arterial disease and renal insufficiency. Nevertheless, the authors concluded that surgical and endovascular treatment may still be warranted in patients with critical limb ischemia and severe renal dysfunction, as the alternative of withholding revascularization might result in even worse outcomes.

In a complementary study, Barshes et al [46] utilized a probabilistic Markov model to simulate the outcomes of various treatment strategies in patients with nonhealing foot wounds and end-stage renal disease. Comparing wound care alone, primary amputation, and various revascularization strategies, this study demonstrated that either local wound care or endovascular therapy might be more cost-effective than primary amputation. By avoiding the perioperative risks, deterioration in quality of life, and increased costs of long-term assisted-living associated with amputation, local wound care may be a particularly beneficial strategy in patients who do not have options of revascularization. The authors emphasized that further studies will be needed to delineate the functional outcomes and wound healing rates of patients with end-stage renal disease and nonhealing foot wounds.

## 9. Conclusions

Renal function, as measured by GFR, should feature prominently in the decision making of vascular surgeons when evaluating patients with aortic aneurysms, carotid stenosis, and peripheral arterial disease for possible intervention, as there is a large body of evidence supporting the association between renal dysfunction and adverse postoperative outcomes. As the current literature is mainly comprised of operative results from single-center studies, future investigations are needed to better determine the outcomes after both nonoperative and operative management of vascular disease in patients with moderate or severe CKD.

Moderate CKD results in significant increased morbidity and mortality after open repair of AAAs. As such, it is reasonable to increase the diameter threshold for repair in these patients to 6 cm. In patients with severe renal dysfunction, defined as an eGFR $<30$ mL/min/1.73 $m^2$, open repair of AAAs should probably not be undertaken, although EVAR may be considered for those patients with an AAA $>6$ cm. Endovascular repair of complex aortic aneurysm may result in improved renal outcomes compared to open repair.

Neither carotid endarterectomy nor angioplasty and stenting appears to be warranted in patients with severe renal dysfunction and asymptomatic carotid stenosis, as the 30-day mortality rates appear to be higher than those deemed acceptable in the repair of asymptomatic disease. Patients with renal insufficiency and symptomatic high-grade carotid stenosis have worse surgical outcomes than patients without renal insufficiency; however, medical therapy may confer even worse outcomes than operative intervention. Recommendations for the management of peripheral arterial disease in patients with severe renal dysfunction follow a similar algorithm. While outcomes in patients with severe renal dysfunction are worse than in patients with mild or moderate renal dysfunction, revascularization appears to result in improved outcomes compared to medical therapy or amputation. Strategies to ameliorate the deleterious effects of renal dysfunction on vascular surgery outcomes are needed, and should be a focus of future investigations.

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